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A service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH

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Insulin Resistance and Pre-Diabetes

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Insulin resistance is a silent condition that increases the chances of developing diabetes and heart disease. Learning about insulin resistance is the first step you can take toward making lifestyle changes that will help you prevent diabetes and other health problems.

What does insulin do?

After you eat, the food is broken down into glucose, the simple sugar that is the main source of energy for the body's cells. But your cells cannot use glucose without insulin, a hormone produced by the pancreas. Insulin helps the cells take in glucose and convert it to energy. When the pancreas does not make enough insulin or the body is unable to use the insulin that is present, the cells cannot use glucose. Excess glucose builds up in the bloodstream, setting the stage for diabetes.

Being obese or overweight affects the way insulin works in your body. Extra fat tissue can make your body resistant to the action of insulin, but exercise helps insulin work well.

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How are insulin resistance, pre-diabetes, and type 2 diabetes linked?

If you have insulin resistance, your muscle, fat, and liver cells do not use insulin properly. The pancreas tries to keep up with the demand for insulin by producing more. Eventually, the pancreas cannot keep up with the body's need for insulin, and excess glucose builds up in the bloodstream. Many people with insulin resistance have high levels of

blood glucose and high levels of insulin circulating in their blood at the same time.

People with blood glucose levels that are higher than normal but not yet in the diabetic range have "pre-diabetes." Doctors sometimes call this condition impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), depending on the test used to diagnose it. In a cross-section of U.S. adults aged 40 to 74 tested during the period 1988 to 1994, 33.8 percent had IFG, 15.4 percent had IGT, and 40.1 percent had pre-diabetes (IGT or IFG or both). Applying these percentages to the 2000 U.S. population, about 35 million adults aged 40 to 74 would have IFG, 16 million would have IGT, and 41 million would have pre-diabetes.

If you have pre-diabetes, you have a higher risk of developing type 2 diabetes, formerly called adult-onset diabetes or noninsulin-dependent diabetes. Studies have shown that most people with pre-diabetes go on to develop type 2 diabetes within 10 years, unless they lose 5 to 7 percent of their body weight—which is about 10 to 15 pounds for someone who weighs 200 pounds—by making modest changes in their diet and level of physical activity. People with pre-diabetes also have a higher risk of heart disease.

Type 2 diabetes is sometimes defined as the form of diabetes that develops when the body does not respond properly to insulin, as opposed to type 1 diabetes, in which the pancreas makes no insulin at all. At first, the pancreas keeps up with the added demand by producing more insulin. In time, however, it loses the ability to secrete enough insulin in response to meals.

Insulin resistance can also occur in people who have type 1 diabetes, especially if they are overweight.

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What causes insulin resistance?

Because insulin resistance tends to run in families, we know that genes are partly responsible. Excess weight also contributes to insulin resistance because too much fat interferes with muscles' ability to use insulin. Lack of exercise further reduces muscles' ability to use insulin.

Many people with insulin resistance and high blood glucose have excess weight around the waist, high LDL (bad) blood cholesterol levels, low HDL (good) cholesterol levels, high levels of triglycerides (another fat in the blood), and high blood pressure, all conditions that also put the heart at risk. This combination of problems is referred to as the metabolic syndrome, or the insulin resistance syndrome (formerly called Syndrome X).

Metabolic Syndrome

Metabolic syndrome is defined by the National Cholesterol Education Program as the presence of any three of the following conditions:

- excess weight around the waist (waist measurement of more than 40 inches for men and more than 35 inches for women)

- high levels of triglycerides (150 mg/dL or higher)

- low levels of HDL, or "good," cholesterol (below 40 mg/dL for men and below 50 mg/dL for women)

- high blood pressure (130/85 mm Hg or higher)

- high fasting blood glucose levels (110 mg/dL or higher)

Source: National Cholesterol Education Program, Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), National Heart, Lung, and Blood Institute, National Institutes of Health, May 2001

Note: Other definitions of similar conditions have been developed by the World Health Organization and the Association of Clinical Endocrinologists.

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What are the symptoms of insulin resistance and pre-diabetes?

Insulin resistance and pre-diabetes usually have no symptoms. You may have one or both conditions for several years without noticing anything. If you have a severe form of insulin resistance, you may get dark patches of skin, usually on the back of your neck. Sometimes people get a dark ring around their neck. Other possible sites for these dark patches include elbows, knees, knuckles, and armpits. This condition is called acanthosis nigricans.

If you have a mild or moderate form of insulin resistance, blood tests may show normal or high blood glucose and high levels of insulin at the same time.

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Do you have insulin resistance or pre-diabetes?

Anyone 45 years or older should consider getting tested for diabetes. If you are overweight and aged 45 or older, it is strongly recommended that you get tested. You should consider getting tested if you are younger than 45, overweight, and have one or more of the following risk factors:

- family history of diabetes

- low HDL cholesterol and high triglycerides

- high blood pressure

- history of gestational diabetes (diabetes during pregnancy) or gave birth to a baby weighing more than 9 pounds

- minority group background (African American, American Indian, Hispanic American/Latino, or Asian American/Pacific Islander)

Diabetes and pre-diabetes can be detected with one of the following tests:

A **fasting glucose** test measures your blood glucose after you have gone overnight without eating. This test is most reliable when done in the morning. Fasting glucose levels of 100 to 125 mg/dL are above normal but not high enough to be called diabetes. This condition is called pre-diabetes or impaired fasting glucose, and it suggests that you have probably had insulin resistance for some time. IFG is considered a pre-diabetic state, meaning that you are more likely to develop diabetes but do not have it yet.

A **glucose tolerance** test measures your blood glucose after an overnight fast and 2 hours after you drink a sweet liquid provided by the doctor or laboratory. If your blood glucose falls between 140 and 199 mg/dL 2 hours after drinking the liquid, your glucose tolerance is above normal but not high enough for diabetes. This condition, also a form of pre-diabetes, is called impaired glucose tolerance and, like IFG, it points toward a history of insulin resistance and a risk for developing diabetes.

These tests give only indirect evidence of insulin resistance. The test that most accurately measures insulin resistance is too complicated and expensive to use as a screening tool in most doctors' offices. The test, called the euglycemic clamp, is a research tool that helps scientists learn more about sugar metabolism problems. Insulin resistance can also be assessed with measurement of fasting insulin. If conventional tests show that you have IFG or IGT, your doctor may suggest changes in diet and exercise to reduce your risk of developing diabetes.

If your blood glucose is higher than normal but lower than the diabetes range, have your blood glucose checked in 1 to 2 years.

Lab Tests and What They Show

- **Blood glucose.** High blood glucose may be a sign that your body does not have enough insulin or does not use it well. However, a fasting measurement or oral glucose tolerance test gives more precise information.

- **Insulin.** An insulin measurement helps determine whether a high blood glucose reading is the result of insufficient insulin or poor use of insulin.

- **Fasting glucose.** Your blood glucose level should be lower

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after several hours without eating. After an overnight fast, the normal level is below 100 mg/dL. If it is in the 100 to 125 mg/dL range, you have impaired fasting glucose or pre-diabetes. A result of 126 or higher, if confirmed on a repeat test, indicates diabetes.

- **Glucose tolerance.** Your blood glucose level will be higher after drinking a sugar solution, but it should still be below 140 mg/dL 2 hours after the drink. If it is higher than normal (in the 140 to 199 mg/dL range) 2 hours after drinking the solution, you have IGT or pre-diabetes, which is another strong indication that your body has trouble using glucose. A level of 200 or higher, if confirmed, means diabetes is already present.

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Can you reverse insulin resistance?

Yes. Physical activity and weight loss make the body respond better to insulin. By losing weight and being more physically active, you may avoid developing type 2 diabetes. In fact, a major study has verified the benefits of healthy lifestyle changes and weight loss. In 2001, the National Institutes of Health completed the Diabetes Prevention Program (DPP), a clinical trial designed to find the most effective ways of preventing type 2 diabetes in overweight people with pre-diabetes. The researchers found that lifestyle changes reduced the risk of diabetes by 58 percent. Also, many people with pre-diabetes returned to normal blood glucose levels.

The main goal in treating insulin resistance and pre-diabetes is to help your body relearn to use insulin normally. You can do several things to help reach this goal.

Be Active and Eat Well

Physical activity helps your muscle cells use blood glucose because they need it for energy. Exercise makes those cells more sensitive to insulin.

The DPP confirmed that people who follow a low-fat, low-calorie diet and who increase activities such as walking briskly or riding a bike for 30 minutes, five times a week, have a far smaller risk of developing diabetes than people who do not exercise regularly. The DPP also reinforced the importance of a low-calorie, low-fat diet. Following a low-calorie, low-fat diet can provide two benefits. If you are overweight, one benefit is that limiting your calorie and fat intake can help you lose weight. DPP participants who lost weight were far less likely to develop diabetes than others in the study who remained at an unhealthy weight. Increasing your activity and following a low-calorie, low-fat diet can also improve your blood pressure and cholesterol levels and has many other health benefits.

Scientists have established some numbers to help people set goals that will reduce their risk of developing glucose metabolism problems.

- **Weight.** Body mass index (BMI) is a measure used to evaluate body weight relative to height. You can use BMI to find out whether you are underweight, normal weight, overweight, or obese. Use the Body Mass Index Table to find your BMI.

  o Find your height in the left-hand column.

  o Move across in the same row to the number closest to your weight.

  o The number at the top of that column is your BMI. Check the word above your BMI to see whether you are normal weight, overweight, or obese. If you are overweight or obese, talk with your doctor about ways to lose weight to reduce your risk of diabetes.

Body Mass Index Table

For a printer-friendly version of this table, use the pdf.*

Height (inches)	Normal						Overweight					Obese						
BMI	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36
	Body Weight (pounds)																	
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179	184
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185	190
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191	196
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197	203
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204	209
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216	223
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223	230
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230	236
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236	243
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243	250
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250	257
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258	265
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265	272
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272	280
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279	287
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287	295

Height (inches)	Obese			Extreme Obesity														
BMI	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
	Body Weight (pounds)																	
58	177	181	186	191	196	201	205	210	215	220	224	229	234	239	244	248	253	258
59	183	188	193	198	203	208	212	217	222	227	232	237	242	247	252	257	262	267
60	189	194	199	204	209	215	220	225	230	235	240	245	250	255	261	266	271	276
61	195	201	206	211	217	222	227	232	238	243	248	254	259	264	269	275	280	285
62	202	207	213	218	224	229	235	240	246	251	256	262	267	273	278	284	289	295
63	208	214	220	225	231	237	242	248	254	259	265	270	278	282	287	293	299	304
64	215	221	227	232	238	244	250	256	262	267	273	279	285	291	296	302	308	314
65	222	228	234	240	246	252	258	264	270	276	282	288	294	300	306	312	318	324

66	229	235	241	247	253	260	266	272	278	284	291	297	303	309	315	322	328	334
67	236	242	249	255	261	268	274	280	287	293	299	306	312	319	325	331	338	344
68	243	249	256	262	269	276	282	289	295	302	308	315	322	328	335	341	348	354
69	250	257	263	270	277	284	291	297	304	311	318	324	331	338	345	351	358	365
70	257	264	271	278	285	292	299	306	313	320	327	334	341	348	355	362	369	376
71	265	272	279	286	293	301	308	315	322	329	338	343	351	358	365	372	379	386
72	272	279	287	294	302	309	316	324	331	338	346	353	361	368	375	383	390	397
73	280	288	295	302	310	318	325	333	340	348	355	363	371	378	386	393	401	408
74	287	295	303	311	319	326	334	342	350	358	365	373	381	389	396	404	412	420
75	295	303	311	319	327	335	343	351	359	367	375	383	391	399	407	415	423	431
76	304	312	320	328	336	344	353	361	369	377	385	394	402	410	418	426	435	443

Source: Adapted from *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. The Evidence Report*
* pdf versions require the free Adobe® Acrobat Reader software for viewing

- **Blood pressure.** Blood pressure is expressed as two numbers that represent pressure in your blood vessels when your heart is beating (systolic pressure) and when it is resting (diastolic pressure). The numbers are usually written with a slash—for example, 140/90, which is expressed as "140 over 90." For the general population, blood pressure below 130/85 is considered normal, although people whose blood pressure is slightly elevated and who have no additional risk factors for heart disease may be advised to make lifestyle changes—that is, diet and exercise— rather than take blood pressure medicines. People who have diabetes, however, should take whatever steps necessary, including lifestyle changes and medicine, to reach a blood pressure goal of below 130/80.

- **Cholesterol.** Your cholesterol is usually reported with three values: low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, and total cholesterol. LDL cholesterol is sometimes called "bad" cholesterol, while HDL cholesterol is called "good" cholesterol. To lower your risk of cardiovascular problems if you have diabetes, you should try to keep your LDL cholesterol below 100 and your total cholesterol below 200.

If you have metabolic syndrome, your doctor may recommend weight loss with diet and exercise, as well as medication to lower your cholesterol and blood pressure levels.

Stop Smoking

In addition to increasing your risk of cancer and cardiovascular disease, smoking contributes to insulin resistance. Quitting smoking is not easy, but it could be the single smartest thing you can do to improve your health. You will reduce your risk for respiratory problems, lung cancer, and diabetes.

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Can medicines help?

Two classes of drugs can improve response to insulin and are used by

prescription for type 2 diabetes—biguanides and thiazolidinediones. Other medicines used for diabetes act by other mechanisms. Alpha-glucosidase inhibitors restrict or delay the absorption of carbohydrates after eating, resulting in a slower rise of blood glucose levels. Sulfonylureas and meglitinides increase insulin production.

The DPP showed that the diabetes drug metformin, a biguanide, reduced the risk of diabetes in those with pre-diabetes but was much less successful than losing weight and increasing activity. In another study, treatment with troglitazone, a thiazolidinedione later withdrawn from the market following reports of liver toxicity, delayed or prevented type 2 diabetes in Hispanic women with a history of gestational diabetes. Acarbose, an alpha-glucosidase inhibitor, has been effective in delaying development of type 2 diabetes. Additional studies using other diabetes medicines and some types of blood pressure medicines to prevent diabetes are under way. No drug has been approved by the Food and Drug Administration (FDA) specifically for insulin resistance or pre-diabetes.

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Hope Through Research

Researchers sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases conducted the DPP to find the most effective ways to prevent or delay the onset of type 2 diabetes. Volunteers were recruited from groups known to be at particularly high risk for IGT and type 2 diabetes. The study was designed to compare the effectiveness of lifestyle changes (weight loss through exercise and diet) with drug therapy (metformin). A control group received a placebo and information on diet and exercise. Participants assigned to the intensive lifestyle intervention reduced their risk of getting type 2 diabetes by 58 percent over 3 years. Participants treated with metformin reduced their risk by 31 percent. Metformin is not currently approved for use in preventing diabetes, but the FDA may determine whether to make diabetes prevention an added indication for this drug. In any event, the DPP demonstrates that a healthy diet and exercise are the most effective treatment for insulin resistance and the prediabetic states of IFG and IGT.

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Points to Remember

- Glucose is the simple sugar that is the main source of energy for the body's cells.

- Insulin helps cells take in blood glucose and convert it to energy.

- If you have insulin resistance, your body's cells do not respond well to insulin.

- Insulin resistance is a stepping-stone to type 2 diabetes.

- Lack of exercise and excess weight contribute to insulin resistance.

- Engaging in moderate physical activity and maintaining proper weight can help prevent insulin resistance.

- Insulin resistance plays a role in the development of cardiovascular disease, which damages the heart and blood vessels.

- Controlling blood pressure and LDL cholesterol and not smoking can also help prevent cardiovascular problems.

- The Diabetes Prevention Program confirmed that exercise and a low-calorie, low-fat diet are the best ways to prevent type 2 diabetes.

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The National Diabetes Information Clearinghouse (NDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health under the U.S. Department of Health and Human Services. Established in 1978, the clearinghouse provides information about diabetes to people with diabetes and to their families, health care professionals, and the public. NDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about diabetes.

Publications produced by the clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This fact sheet was reviewed by George A. Bray, M.D., Pennington Biomedical Research Center, Louisiana State University; and Richard F. Hamman, M.D., Dr.P.H., Department of Preventive Medicine and Biometrics, University of Colorado Health Sciences Center.

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